contained in each discrete region are at least about 50 subunits in length, which are individually applied to each region in the microarray.

REMARKS

The Amendment

The specification is amended to insert a paragraph regarding the colored drawings, as required by MPEP.

Claim 7 is amended to delete the phrase regarding cross-contamination.

No new matter is added in any of the above amendments. The Examiner is requested to enter the amendment and reconsider the application.

The Response

Formal Drawings

Applicants are submitting herewith a set of color drawings with a Petition and the requisite fee. Applicants believe that the colored drawings as submitted meet the requirements of 37 C.F.R. §1.84.

35 U.S.C. §112, First Paragraph Rejection

Claims 7-20, 34, 35, 38, and 39 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states that the claims contain new matter in that there is no written basis for the generic phrase "each region in the microarray is essentially free of cross-contamination with...".

Applicants respectfully submit that the limitation "free of cross-contamination" is not a new matter because such feature is an inherent characteristic when a DNA solution is individually applied to each region of the microarray. However, to further prosecution,

Applicants have deleted such phrase. In view of the claim amendments, the new matter rejection of Claims 7-20, 34, 35, 38 and 39 should be withdrawn.

Consequently, all pending Claims 7-40 are entitled to the priority date of the earliest parent application, which is June 17, 1994

35 U.S.C. §102(e) Rejection

1. Claims 7-20, 34, 35, 38, and 39 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Lipshutz, *et al.* (U.S. Patent No 6,013,440).

As discussed above, the instant application is entitled to the priority date of June 17, 1994. Therefore, Lipshutz, *et al.*, which was issued on June 11, 2000 and has claimed a priority of March 11, 1996, does not qualify as a §102(e) reference.

2. Claims 7, 11-15, 17, 18, 20, and 34 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Dehlinger (U.S. Patent No. 5,723,320).

As discussed above, the instant application is entitled to a priority date of June 17, 1994. Therefore, Dehlinger, which was issued on March 3, 1998 and filed on August 29, 1995 does not qualify as a §102(e) reference.

35 U.S.C. §103(a) Rejection

Claims 7-40 are rejected under 35 U.S.C. §103(a) as being unpatentable over Pirrung, *et al.* (WO 90/15070). The rejection is traversed because Pirrung, *et al.*, do not teach or suggest a microarray of DNA sequences, which are at least about 50 subunits in length and are individually applied to each region in the microarray.

1. DNA Sequences of at least 50 subunits

Pirrung, *et al.* disclose a substrate having a plurality of polymer sequences in predefined regions (page 14, line 32). The reference primarily teaches a method of large-scale immobilized peptide synthesis. Nucleic acids are only listed as one example among many other possible polymers such as polysaccharides, phospholipids, peptides having either α-, β-, or ω-amino acids, heteropolymers in which a known drug is covalently bound to any of the above, polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines,

polyarylene sulfides, polysiloxanes, polyimides, polyacetates, or other polymers (see page 14, line 25 through page 15, line 7). There is no disclosure at all in the reference regarding a microarray of DNA sequences, wherein the DNA sequences contained in each discrete region are at least about 50 subunits in length (Claims 7-20, and 34-39); therefore, it is not possible that the reference would have an enabling disclosure as to how to prepare such a microarray.

Further, the Examiner is mistaken in stating (Office Action at page 7):

> "It is noted that non-covalent immobilization of nucleic acids may also occur via the receptor polynucleotide binding to immobilize sample nucleic acids as discussed in the reference on page 19, lines 13-23. Such nucleic acids are well known to be optimally oligomers as well as gene length, or even a whole chromosome of millions of bases in length. Thus, clearly immobilization of sequences of 50 or more bases as in claim 7 is included as being suggested and motivated by the reference."

Applicant respectfully submits that the Examiner has misinterpreted the reference. At page 19, lines 13-23, the reference states that the invention may be used in immobilization of cells, proteins, lectins, nucleic acids, polysaccharides, and the like in patterns on a surface via molecular recognition of specific polymer sequences. The reference discloses that nucleic acids may bound to a substrate that has specific polymer sequences on the surface. **The polymer is part of the substrate; the immobilized nucleic acids are not part of the substrate.** There is no disclosure in the reference of a substrate with a surface comprising a microarray of DNA sequences, wherein the DNA sequences are at least about 50 bases in length, which are individually applied to each region in the microarray.

The instant microarray of DNA sequences having at least 50 bases has an additional advantage in that the microarray sequences can selectively hybridize with specific polynucleotides in a polynucleotide mixture. Microarray DNA sequences that have relatively short oligonucleotides (such as 8-10 bases) cannot selectively hybridize with a specific polynucleotide sequence in a mixture (see page 13, lines 7-16).

2. Cross-Contamination

Further, Pirrung, *et al.* only teach synthesizing polymers (peptides) from monomers on the substrate; Pirrung, *et al.* do not teach or suggest individually applying DNA to each region in the microarray. Therefore, the inherent characteristics of the reference microarray substrate and the instant microarray substrate are different. The microarray of the present invention (Claims 7-40) is inherently free of cross-contamination because the DNA solution is individually applied to each region. Whereas the reference microarray is likely to be cross contaminated, as conceded in a much later filed U.S. Patent 5,744,305, which is a continuation-in-part application of the reference. For example, Column 17, line 59-67 of the '305 Patent describes:

> "Another important consideration is the fidelity of synthesis. Deletions are produced by incomplete photodeprotection or incomplete coupling. The coupling yield per cycle in these experiments is typically between 85% and 95%. Implementing the switch matrix by masking is imperfect because of light diffraction, internal reflection, and scattering. Consequently, stowaways (chemical units that should not be on board) arise by unintended illumination of regions that should be dark."

Applicants respectfully submit that in the Office Action at page 6, the Examiner is mistaken in stating that "these regions are formed of substantially pure polymers, as noted on page 14, lines 18-26, which suggest that the formation of these regions occurs in a process which is essentially free of cross-contamination." The cited passage of the reference only describes the definition of "substantially pure." There is no evidence or any indication that the reference substrate has a substantially pure polymer within a predefined region. As a matter of fact, the later filed '305 Patent has admitted that the reference microarray has an intrinsic problem of cross-contamination (see above).

For the reasons stated above, the 103(a) rejection of Claims 7-40 over Pirrung, *et al.*, should be withdrawn.

CONCLUSION

Applicants believe that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 463-8181.

Respectfully submitted,

Date: March 3, 2003

Glenn Rhodes (Reg. No. 31,790)
Viola T. Kung (Reg. No. 41,131)
Karen K. Wong (Reg. No. 44,409)

HOWREY SIMON ARNOLD & WHITE, LLP
301 Ravenswood Avenue
Box No. 34
Menlo Park, CA 94025
(650) 463-8181

MARKED-UP VERSION SHOWING CHANGES MADE IN THE CLAIMS

7. (Three Times Amended) A substrate with a surface comprising a microarray of DNA sequences, wherein (i) the microarray has a density of about 400 or more discrete regions of DNA sequences per cm^2 of substrate surface, (ii) the DNA sequences are isolated polynucleotides, (iii) the microarray comprises 400 or more regions, and (iv) the DNA sequences contained in each discrete region are at least about 50 subunits in length, [each region in the microarray is essentially free of cross-contamination with DNA sequences] which are individually applied to [the other regions] each region in the microarray.